CONDITIONAL PETITION FOR EXTENSION OF TIME

If entry and consideration of the amendments above requires an extension of time, Applicants respectfully request that this be considered a petition therefor. The Commissioner is authorized to charge any fee(s) due in this connection to Deposit Account No. 14-1263.

ADDITIONAL FEE

Please charge any insufficiency of fees, or credit any excess, to Deposit Account No. 14-1263.

REMARKS/ARGUMENTS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

Claims 1 and 2 have been amended to make clear that "each of" the lysates comprises a plurality of proteins expressed by the respective cell populations. This language finds clear support throughout the specification and is not believed to introduce new matter. An early notice to that effect is earnestly solicited.

Claims 1, 3-5, 12, 15, 20, 23, 26, 28, 33 and 69 were rejected under 35 USC § 102(b) as being anticipated by Kamb, US 2003/0027214. In response, Applicants renew their position that Kamb does not, in fact, anticipate any of the rejected claims.

Applicants previously argued that Kamb does not teach "lysates comprising a plurality of proteins expressed by the respective cell populations," as required by the previous claims. The Examiner alleged in the paragraph bridging pages 38-39 of the final rejection that the claims did not exclude an array of single polypeptides at each array location. Applicants disagree, but, in order to advance the prosecution, Applicants have amended claim 1, and, therefore, the remaining rejected claims, to require that *"**each of** the lysates [comprise] a plurality of proteins expressed by the respective cell populations. Applicants respectfully submit that this language expressly excludes the possibility that any of the lysates can contain only a single polypeptide.

The Examiner mentions also on page 38 that Kamb teaches one *type* of cells and thus one

type of polypeptide per array location and that a concentration of the unique polypeptide from multiple single-cell clones implies that there are more than one polypeptide in the lysate per array location. What the Examiner means is not entirely clear. If the Examiner means that a "concentration of a peptide" in Kamb implies that there is more than one molecule of this peptide in the lysate then Applicants agree with this assumption. However, if the Examiner means a "concentration of a peptide" means "molecules of chemically different peptides" then Applicants do not agree.

Applicants respectfully submit that it would have been clear to any person skilled in this art that "a unique" or "one" polypeptide in the context of Kamb means that the procedure of Kamb's paragraph [0054] aims to increase this concentration/quantity of a particular peptide (or peptide *type*) of interest inside a well. Cloning and lysing of cloned cells aim to increase the concentration above the limit of sensitivity of used detection method which improves reliability of measurements for this peptide.

When Kamb describes that "in some embodiments a unique polypeptide [...] may be adhered to a location-determinable support, [...] prior to exposure to the ligands" [0024] and then further that: "This location-determinable support may be a solid support that is suitable for adhering a desired polypeptide from a polypeptide-containing lysate, and which can be correlated back to a particular polypeptide source – e .g a particular well in a particular array," [0032], it would be clear to any person skilled in the art that "unique" means only chemically identical polypeptides (one polypeptide *type*) may adhere to the support.

The Examiner also argues that the generation of lysate plates as described by Kamb in paragraph [0054] is encompassed by lines 3-4 of the previous claim. Certainly, Kamb does not describe what is presently claimed. Kamb also do not describe what was previously claimed. The procedure required by previous claim 1 involved depositing at discrete sites small quantities of the cell lysates as deposited samples, in diluted or undiluted for directly on said solid support, thereby creating one or more one- or two-dimensional arrays of discrete measurement areas on said solid support.

Kamb is definitely different from this. First, the arrays of Kamb's wells are not arrays of discrete measurement areas defined as a surface of deposited lysate as in the present invention [0062]. Second, in the method of Kamb, library arrays are generated in which each well produces a unique polypeptide (*type*) [0052]. Kamb teaches that for analysis of a different cell population each lysate is either kept segregated in a unique location (a well) or exposed to a solid support that is unique to that lysate source [0032]. Used solid supports are described in [0033] and can be taken off the well so that remaining proteins are removed before applying ligands. So the adhesion of Kamb does not lead to the creation of discrete measurement areas in one or more one- or two dimensional arrays on a solid support. Paragraph [0054] only describes enrichment by cloning and transfer of lysate to a unique array location. It is clear to persons skilled in the art that this unique location is a well as mentioned in [0031]. The fact that the contents of several cell clones and not the content of a single-cell clone are transferred to a unique array location does not change the essential teaching of Kamb that a unique polypeptide (*type*) from the concentrated lysate of [0054] adheres on a support according to Kamb in paragraphs [0024] and

[0032]. The adhesion is therefore limited to a unique polypeptide (*type*) and other proteins present in the lysate in small concentration do not adhere.

In short, Kamb only teaches that a lysate is deposited on one support suitable for adhering a desired polypeptide (*type*) from the lysate so one polypeptide (*type*) is immobilized on one support. Kamb does not teach or suggest the present invention, wherein one support comprises a plurality of measurement areas defined by the closed area that is occupied by deposited lysates [0062] comprising a plurality of chemically different proteins (*types*) so that the whole lysate is immobilized.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has been reconsidered and withdrawn is earnestly solicited.

Claims 2, 6-8, 14 and 29 were rejected under 35 USC § 103(a) as being obvious over Kamb. In response, Applicants again respectfully submit that Kamb does not make out a *prima facie* case of the obviousness of the rejected claims.

As pointed out previously, the Examiner concedes that Kamb does not teach providing lysates from more than one population of cells. However, the Examiner finds that providing a second population of cells in the array would have been obvious because the desirability of such simultaneous screening is well known in the art and is also discussed by Kamb in paragraph [0005].

In response, Applicants again respectfully disagree that a person having ordinary skill in the art would, in fact, have been so motivated. Indeed, Applicants respectfully submit that such a person would not have had any motivation to modify the teaching of Kamb in immobilizing a plurality of proteins expressed by a cell population because he would have expected to lose the possibility to identify protein/ligand pair by tracing unique array location [0052]. Consequently, such a person would not, in fact, have been motivated to make the modifications in Kamb necessary to achieve the invention of the rejected claims.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claims 9 and 11 were rejected under 35 USC § 103(a) as being obvious over Kamb in view of Shen et al. ("Shen"), US 6,458,829. In response, Applicants again respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Shen overcomes the above-noted deficiencies of Kamb. Indeed, Shen only mentions in-vitro assays for selection and screening of anti-inflammatory compounds and cellular assays for in-vitro study of inflammation reaction in general.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claim 10 was rejected under 35 USC § 103(a) as being obvious over Kamb in view of Gundersen et al. ("Gundersen"), US 20030129749. In response, Applicants again respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Gundersen overcomes the above-noted deficiencies of Kamb. Indeed, Gundersen only describes comparison of diseased and healthy cell population is.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claim 13 was rejected under 35 USC § 103(a) as being obvious over Kamb in view of Oh et al. ("Oh"), US 5,863,742. In response, Applicants again respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Oh overcomes the above-noted deficiencies of Kamb. Indeed, Oh only describes addition of an intracellular protein to the analyte of the cell lysate for control.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claims 16-19, 24 and 25 were rejected under 35 USC § 103(a) as being obvious over Eipel et al. ("Eipel"), US 6,737,024, in view of Kamb. In response, Applicants again respectfully

submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Eipel overcomes the above-noted deficiencies of Kamb. Indeed, although the Examiner considers the hydrophobic coating of Eipel and the adhesion-promoting layer of the rejected claims to be equivalent, Applicants disagree.

The hydrophobic coating of Eipel prevents the measurement zone spreading into one another, providing a "wall" to chemically defined wells of pm-size, thereby solving the problem of increasing capillary forces in pm-sized wells. Reagents or cells are placed on the measurement points on the support surface and bring about reaction thereof. Proteins or nucleic acid can be present in adsorbed or in chemically bound form (col. 4, 1. 59-col 5, 1. 4). Further details on how chemical binding may be achieved are not given.

The purpose of the adhesion-promoting layer of the present invention is to improve adhesion of the proteins contained in the deposited lysates in comparison to purely adsorptive immobilization on the surface of the support (p. 16, 1 3).

In other words the adhesion-promoting layer of the embodiments of the rejected claims enhance the chemical binding of proteins within measurement areas, whereas the hydrophobic coating of Eipel only defines the outer limits of measurement areas.

The hydrophobic coating of Eipel and the adhesion-promoting layer of rejected claims are, therefore, not equivalent. As binding proteins is not an issue of Eipel, persons having ordinary skill in the art would not have been motivated to combine Kamb and Eipel. And, had he

done so, he would rather have been motivated to replace classic well-plates used by Kamb by chemically defined well-plates of Eipel in order to minimize volumes but certainly would not have been motivated to modify the immobilization of the proteinaceous analytes of Kamb.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claims 21 and 22 were rejected under 35 USC § 103(a) as being obvious over Kamb in view of Craig et al. ("Craig"), US 6,972,198. In response, Applicants again respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Craig overcomes the above-noted deficiencies of Kamb. Indeed, Craig only describes an immobilization assay wherein adhesion of one protein on the surface of a solid support is achieved using an adhesion moiety as described by Kamb [col. 19,1. 25-col. 20, 1. 7]. Craig also teaches this concept of immobilized assay can be applied to measure the activities of multiple post-translational modification enzymes in a complex sample [Assay 6, col. 20, 1. 11-16] that is to a plurality of proteins to be analyzed simultaneously. However the solution of Craig comprises a common peptide partner or a specific partner for each target protein immobilized on a solid support. The sample (e.g. the lysate) is then added to the immobilized array of specific binding partners [col. 20, 1.23 to 26] allowing the separation of the proteins of interest from the rest of the lysate.

This is not the immobilized assay of the rejected claims wherein a plurality of proteins are deposited directly on solid support or on an adhesion-promoting layer without modification or separation of the proteinaceous analytes.

A person having ordinary skill in the art would not have been motivated to modify the method of Craig for a plurality of proteins as he would have lost selective binding of proteins of interest on the support.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claim 27 was rejected under 35 USC § 103(a) as being obvious over Kamb in view of Matson et al. ("Matson"), US 7,070,740. In response, Applicants again respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Matson overcomes the above-noted deficiencies of Kamb. Indeed, Matson only teaches that well plates for assays can be used for trans- or epi-illumination reading using the architecture of Kamb.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claims 30-32 were rejected under 35 USC § 103(a) as being obvious over Kamb in view

of Lackritz et al. ("Lackritz"), US 6,956,651. In response, Applicants again respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Lackritz overcomes the above-noted deficiencies of Kamb. Indeed, Lackritz teaches an array architecture wherein the support sensor is coated with a member of a binding pair (MBP), chosen because they interact exclusively with a selected target, analyte or molecule of a sample. When the support sensor is exposed to a sample that contains analyte molecules, they bind to the sensors surface via their specific interaction with MBP. Detection is achieved by comparison of the observed surface plasmon resonance shift with a stored calibration curve.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claims 34-41 were rejected under 35 USC § 103(a) as being obvious over Kamb in view of Duveneck et al. ("Duveneck"), US 6,395,558. In response, Applicants again respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Duveneck overcomes the above-noted deficiencies of Kamb. Indeed, Duveneck only discloses an optical wave guide on which the architecture also described by Kamb is allegedly applied.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,
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